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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,040	11/21/2006	Bin Wang	133232.00201	5612

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EXAMINER	
GANGLE, BRIAN J	
ART UNIT	**PAPER NUMBER**
1645	

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12/31/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,040	WANG ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9-12 and 20-35* is/are pending in the application.

4a) Of the above claim(s) *22-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 9-12, 19-21, and 30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/28/2009 has been entered.

The amendment and remarks, filed 10/28/2009, are acknowledged. Claims 1, 9-12, 20-23, and 30-35 are amended. Claims 1, 9-12, and 20-35 are pending. Claims 22-29 are withdrawn as being drawn to non-elected inventions. Claims 1, 9-12, 19-21, and 30-35 are currently under examination.

Rejections Withdrawn

The rejection of claims 1, 9-12, 20-21, and 30-35 under 35 U.S.C. 103(a) as being unpatentable over Wen *et al.* (US Patent 6,221,664, 4/2001), is withdrawn upon further consideration and in light of the new rejection set forth below.

The rejection of claims 1, 9-12, 19-21, and 30-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pundi *et al.* (WO 02/078732 A1, 10/2002), is withdrawn upon further consideration and in light of the new rejection set forth below.

Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 10-12, 20, and newly submitted claims 30-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 10, and 11 of copending Application No. 11/644,435, for the reasons set forth in the previous office action.

Applicant argues:

That the rejection should be withdrawn since all the other rejections have been obviated and this is the only remaining rejection.

Applicant's arguments have been fully considered and deemed non-persuasive.

According to MPEP 804:

Where this issue can be addressed without violating the confidential status of applications (35 U.S.C. 122), the courts have sanctioned the practice of making applicant aware of the potential double patenting problem if one of the applications became a patent by permitting the examiner to make a "provisional" rejection on the ground of double patenting. *In re Mott,* 539 F.2d 1291, 190 USPQ 536 (CCPA 1976); *In re Wetterau,* 356 F.2d 556, 148 USPQ 499 (CCPA 1966). The merits of such a provisional rejection can be addressed by both the applicant and the examiner without waiting for the first patent to issue.

The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in at least one of the applications.

Therefore, the rejection is proper and is maintained.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending Application No. 11/644,435 are drawn to a composition comprising a eukaryotic cell expression vector containing nucleotide sequences encoding an allergenic protein or a polypeptide that comprises an antigenic epitope of said allergenic protein and the protein or polypeptide that comprises an antigenic epitope of said

protein. Said vector comprises an RSV, CMV, or SV40 promoter and the vector is in proportion to the protein in a ratio of 1:5 to 5:1.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

New Claim Rejections

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9-12, 19-21, and 30-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to compositions comprising a nucleic acid eukaryote cell expression carrier encoding a targeted antigen and the targeted antigen, wherein the ratio of carrier is 5:1, from 2:1 to 10:1, from 1:5 to 5:1, or from 1:2 to 1:10, and wherein the composition must inhibit a Th1 T-cell immune response. The claims encompass compositions comprising any antigen, not only from every pathogen in the world, but also from every organism in the world, including self antigens, tumor antigens, plant, protozoan, bacterial, and viral antigens.

The specification asserts that a composition comprising a protein antigen and the DNA that encodes it is a T-cell immune response inhibitor, specifically, a Th1 inhibitor. However, the specification does not disclose any example where inhibition of a Th1 T-cell response was shown. The specification discloses several examples where bovine foot and mouth disease virus (FMDV) antigen VP1 and an expression vector encoding VP1 were administered to mice, as well as various treatments such as VP1 protein alone, VP1 vector alone, whole virus vaccine alone, or VP1 protein followed by VP1 vector at 14 days or vice versa. The combination of protein and expression vector elicited the same level of antibodies as the other treatments. The

combination of protein and expression vector led to T-cell expansion in every case. The level of T-cell expansion was less than that induced by either the protein or the vector alone, but T-cell expansion was shown. There were no tests performed that looked specifically at Th1 cells or any specific type of Th1 cell activity. Therefore, the specification lacks description of any composition that meets the limitations of the claims.

The art does not provide any support for the notion that a protein antigen mixed with the DNA encoding it is a Th1 inhibitor. The idea of mixing antigens with the DNA encoding them is not novel and has been disclosed by several authors as a vaccine. Pundi *et al.* (WO 02/078732 A1, 10/2002) disclose a vaccine formulation comprising a DNA vaccine that encodes a polypeptide of a virus as well as the inactivated virus (see abstract). Wen *et al.* (US Patent 6,221,664, 4/2001) disclose a vaccine comprising hepatitis B surface antigen as well as plasmid DNA which encodes said antigen and an adjuvant (see column 5, lines 1-26). In fact, in column 3, Wen states that interferon-γ was increased by administration of the composition. As interferon-γ is the signature cytokine of Th1 cells, it appears that the composition of Wen actually increases the Th1 response. Shrivastava *et al.* (Vaccine, 27:6582-6588, 2009) used hepatitis E or B antigens mixed with the DNA encoding them to immunize mice and found an increase in the Th1 response (see section 3.3.1 and page 6587, column 1, final paragraph and column 2, paragraph 2).

To meet the limitations of the claims, the compositions must *inhibit* a Th1 cell response. Inducing a lesser response than a standard vaccine is not inhibition; in fact it is the opposite of inhibition. The specification, the art, and applicant's arguments show that there is no correlation between the structural features of the claimed invention and the function of the claimed invention. Simply combining a protein antigen with DNA encoding it does not inhibit the Th1 response, and the specification provides no description of any composition that does so.

Claims 1, 9-12, 19-21, and 30-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims are drawn to compositions comprising a nucleic acid eukaryote cell expression carrier encoding a targeted antigen and the targeted antigen, wherein the ratio of carrier is 5:1, from 2:1 to 10:1, from 1:5 to 5:1, or from 1:2 to 1:10, and wherein the composition must inhibit a Th1 T-cell immune response.

Breadth of the claims: The claims encompass compositions comprising any antigen, not only from every pathogen in the world, but also from every organism in the world, including self antigens, tumor antigens, plant, protozoan, bacterial, and viral antigens.

Guidance of the specification/The existence of working examples: The specification asserts that a composition comprising a protein antigen and the DNA that encodes it is a T-cell immune response inhibitor, specifically, a Th1 inhibitor. However, the specification does not disclose any example where inhibition of a Th1 T-cell response was shown. The specification discloses several examples where bovine foot and mouth disease virus (FMDV) antigen VP1 and an expression vector encoding VP1 were administered to mice, as well as various treatments

such as VP1 protein alone, VP1 vector alone, whole virus vaccine alone, or VP1 protein followed by VP1 vector at 14 days or vice versa. The combination of protein and expression vector elicited the same level of antibodies as the other treatments. The combination of protein and expression vector led to T-cell expansion in every case. The level of T-cell expansion was less than that induced by either the protein or the vector alone, but T-cell expansion was shown. There were no tests performed that looked specifically at Th1 cells or any specific type of Th1 cell activity.

State of the art: The art does not provide any support for the notion that a protein antigen mixed with the DNA encoding it is a Th1 inhibitor. The idea of mixing antigens with the DNA encoding them is not novel and has been disclosed by several authors as a vaccine. Pundi *et al.* (WO 02/078732 A1, 10/2002) disclose a vaccine formulation comprising a DNA vaccine that encodes a polypeptide of a virus as well as the inactivated virus (see abstract). Wen *et al.* (US Patent 6,221,664, 4/2001) disclose a vaccine comprising hepatitis B surface antigen as well as plasmid DNA which encodes said antigen and an adjuvant (see column 5, lines 1-26). In fact, in column 3, Wen states that interferon-γ was increased by administration of the composition. As interferon-γ is the signature cytokine of Th1 cells, it appears that the composition of Wen actually increases the Th1 response. Shrivastava *et al.* (Vaccine, 27:6582-6588, 2009) used hepatitis E or B antigens mixed with the DNA encoding them to immunize mice and found an increase in the Th1 response (see section 3.3.1 and page 6587, column 1, final paragraph and column 2, paragraph 2).

In addition to the teachings of the specification and the art, which show an increase in the Th1 response rather than inhibition of the Th1 response, applicant's own arguments show that the claims are not enabled. As discussed above, both Wen *et al.* and Pundi *et al.* disclose compositions that meet the structural limitations of the claims. However, applicant has argued the use of these references in art rejections stating that the compositions do not have the required Th1 inhibition activity.

To meet the limitations of the claims, the compositions must *inhibit* a Th1 cell response. Inducing a lesser response than a standard vaccine is not inhibition. The specification, the art, and applicant's arguments show that simply combining a protein antigen with DNA encoding it does not inhibit the Th1 response, and the specification provides no guidance on any

composition that does so. Therefore, in view of the lack of support in the art and specification, it would require undue experimentation on the part of the skilled artisan to make and use the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian J Gangle/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645